

A Novel Asymmetric Synthesis of (-)-*cis*-1, 3-Dibenzylhexahydrofuro[3, 4-d]imidazole-2,4-dione

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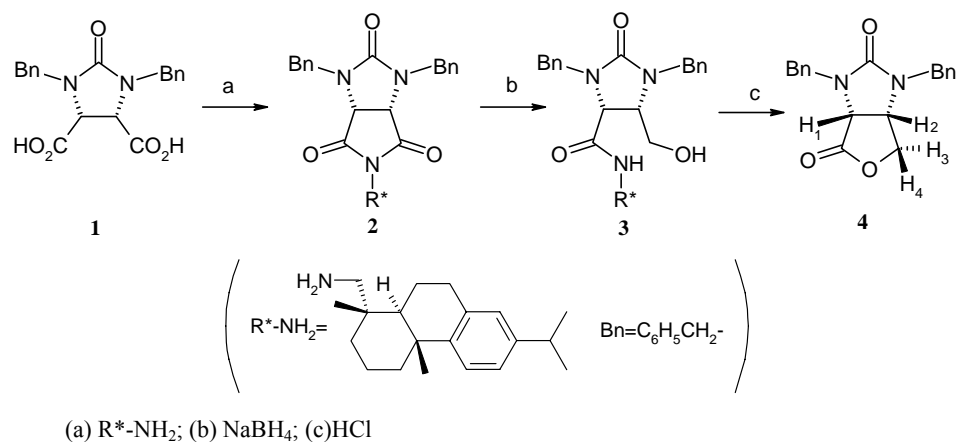
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Abstract: (-)-*cis*-1, 3-Dibenzyl-hexahydrofuro[3, 4-d]imidazole-2, 4-dione was prepared by a new synthesis method from meso dicarboxylic acid and dehydroabietylamine by asymmetric reduction in good yield with up to 91.6% e.e. value.

Keywords: Synthesis, lactone, dehydroabietylamine, reduction, asymmetric.

Desymmetrisation of meso-compounds enables a rapid access to very useful chiral materials possessing multiple asymmetric centers. In this respect, a useful class of starting materials is cyclic imides, such as the synthesis of optical activated *cis*-1, 3-dibenzylhexahydrofuro [3, 4-d] imidazole-2, 4-dione. Up to now, the synthesis of (+)-*cis*-1, 3-dibenzylhexahydrofuro[3, 4-d]imidazole-2, 4-dione (this compound being herein after referred to as (+)-lactone) as an important intermediate of d-biotin have been reported in a lot of methodologies¹, but the synthesis of (-)-*cis*-1, 3-dibenzylhexahydrofuro[3, 4-d]imidazole-2, 4-dione (this compound being herein after referred to as (-)-lactone) has scarcely been reported. Here we report a new synthesis method of (-)-lactone as showed in **Scheme 1**.

Scheme 1 The asymmetric synthesis of optical lactone



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Starting from *cis*-1, 3-dibenzyl-2-oxo-imidazolidine-4, 5-dicarboxylic acid **1**, the compound **2** was prepared in good yield by dehydration from **1** and dehydroabietylamine. Followed by selective reduction of carbonyl group by NaBH₄, compound **2** was converted to hydroxy amide **3**. Subsequent hydrolyzation by HCl and then refluxing to dehydration, we obtained lactone **4** in good yield with up to 91.6% e.e. value. The product **4** was purified by recrystallization and characterized by IR, ¹HNMR. The spectral data were identical with that of the (+)-lactone, but e.e. value was just reverse to that of (+)-lactone.

Acknowledgment

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References and Notes

1. P. J. De Clerq, *Chem. Rev.*, **1997**, *97*, 1755.
2. For compound **4**, mp 109-110°C; [α]_D²⁰ -54.1 (c 1, CHCl₃); ¹HNMR (500MHz, CDCl₃, δ ppm): 7.31-7.38(m, 10H, 2C₆H₅-), 5.03(d, 1H, *J*=14.77Hz, H-3), 4.62(d, 1H, *J*=15.15Hz, H-2), 4.37 (t, 2H, *J*=28.67Hz, H-1, H-4), 4.15(s, 4H, 2Ph-CH₂-); IR (KBr, cm⁻¹): 3414, 2920, 1772, 1706.9, 1637, 1617, 1415, 1211, 753, 702.

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